UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/380,310	08/31/1999	KOJI UKAI	0425-0736P	2449

2292 7590 12/29/2008

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
HAGHIGHATIAN, MINA	
ART UNIT	PAPER NUMBER
1616	

NOTIFICATION DATE	DELIVERY MODE
12/29/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	09/380,310	UKAI ET AL.	
	Examiner	Art Unit	
	MINA HAGHIGHATIAN	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09/16/08*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22,41,62 and 64-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22,41,62 and 64-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of the Amendments and Remarks filed on 09/16/08 Claims 41 and 68 have been amended while no claims have been cancelled or newly added. Accordingly claims **22, 41, 62 and 64-68** remain pending.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 22, 41, 62, 65-66 and 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tai (5,013,557) in view of Matoba et al (5,464,612) and further in view of Kawakami et al (The Rational for E2020 as a potent acetylcholinesterase inhibitor)

Tai discloses taste masking compositions comprising spray dried microcapsules containing sucralfate and methods for preparing same. The spray dried spheroidal microcapsules comprise in percentages by weight between 1 and 70% of **sucralfate** and between 30 and 99% of a polymer soluble in gastric fluids (col. 5, lines 30-60). The **polymers** soluble in the gastric fluids are polymers which **bind** to **sucralfate** with taste masking properties and **dissolve in gastric fluid**. The suitable polymers include alginic acid, **carrageenan**, xanthan, polyvinylpyrrolidone, etc (col. 6, lines 26-55). It is disclosed that sucralfate is well known in the art as a **basic** aluminum sucrose sulfate complex (see col. 1, lines 45-47 and col. 6, lines 8-12). The formulations may be made into tablets, chewable tablets and spheroidal microcapsules (col. 5, lines 40-50). Tai lacks specific disclosure on donepezil hydrochloride.

Matoba et al teach a clad powdery or granular preparation of a medicinally active ingredient and a powdery or granular ion exchanger blended to prepare a solid preparation. The active agents are **basic** compounds (see abstract). It is also disclosed that the medicinally active ingredients having an unpleasant taste and/or odor may frequently have a basic group (col. 4, lines 37-39). While Matoba et al does not specifically list donepezil as one of the active agents, it is known in the art that donepezil is a basic compound.

Kawakami et al teach E2020 (also known as donepezil hydrochloride) as a potent acetylcholinesterase inhibitor. E2020 was developed for treatment of Alzheimer's disease, and possibly other dementias.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have modified the formulations of Tai containing a basic medicine with unpleasant taste and an acidic polysaccharide such as carrageenan with other active agents such as donepezil hydrochloride as taught by Kawakami et al in order to prepare more drug formulations with a masked taste for patient convenience and to increase patient compliance. Matoba et al disclose that typically the basic active agents have a bitter taste. In other words, one or ordinary skill in the art having the formulations of Tai and knowing that basic drugs have a bitter taste, would have been motivated to apply the same method to other medications with unpleasant taste in order to provide better tasting medication for patients and increase patient compliance. Additionally, the claims would have been obvious because the technique for improving a particular method was part of the ordinary capabilities of a person of ordinary skill in the art, in view of the teaching of the technique for improvement in other situations.

Claims 64 and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tai (5,013,557) in view of Matoba et al (5,464,612) and further in view of Kawakami et al (The Rational for E2020 as a potent acetylcholinesterase inhibitor)

as applied to claims 22 and 65-66 above, and further in view of Morikazu et al (JP 4-346937).

The combined references, discussed above, lack specific disclosure on derivatives of carrageenan.

Morikazu teaches a method of simply and economically reducing bitterness of drugs and foods. For that, Morikazu mixes a bitter substance with a gelatininzing agent such as gelatin, *k*-carrageenan, etc and a seasoning agent, preferably a sweetener (see abstract).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made given the general teachings of binding a polymer with a basic active agent of Tai, to have looked in the art for specific agents such as *k*-carrageenan suitable for said formulations as taught by Moikazu with a reasonable expectation of successfully preparing a safe and effective drug formulation without a bitter or unpleasant taste for patients that need such medicaments. In other words, the claims would have been obvious because the substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims **22, 41, 62 and 64-68** are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 6, 12 of U.S. Patent No. **6,576,677** in view of Tai (5,013,557). Claims 22, 41, 62 and 64-68 are not patentably distinct from the reference claims because the claims would have been obvious over the reference claims in view of Tai reference. Specifically, the instant claims are drawn to an oral medicine comprising donepezil hydrochloride and an acidic polysaccharide. The reference claims are drawn to an oral medicine comprising an active agent such as donepezil hydrochloride and a component such as polyvinylpyrrolidone. Tai teaches a method of making the bitter taste of sucralfate by binding it to a polymer such as carrageenan or polyvinylpyrrolidone. Thus it is taken that

Tai is teaching that carrageenan and polyvinylpyrrolidone are equivalent and would have lead one of ordinary skill to the same product. Therefore, the claims would have been obvious because the substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Response to Arguments

Applicant's arguments filed 09/16/08 have been fully considered but they are not persuasive.

Applicant argues that "Tai, at column 6, lines 36-44, discloses many compounds as useful in producing spray-dried microcapsules of sucralfate. However, there are no examples using the referenced compounds". This is not persuasive. Tai discloses polymers soluble in gastric fluids useful in the present invention are those polymers that will bind to sucralfate. Suitable polymers include maltodextrins, carrageenan and polyvinylpyrrolidone. Example 1 in column 20 prepares spray-dried spheroidal microcapsules by dissolving Maltrin (tradename for maltodextrin) in water and then suspending sucralfate in the Maltrin solution.

Applicant then argues that sucralfate is an acidic compound and not a basic compound. It is stated that "sucralfate is a basic aluminum sucrose sulfate having a negative charge, and therefore does not form a complex by an ionic interaction as is formed in the claimed invention. In fact the mechanism for masking a bitter taste of sucralfate is different". This is not persuasive. It has been shown that Tai teaches preparation of dosage forms with masked bitter or unpleasant taste by binding a

polymer with the bitter active compound. This is what the present Application is accomplishing too. The fact that sucralfate is not a basic medicament or that a complex is not formed is not commensurate with the scope of claims. The instant claims are drawn to compositions comprising a basic medicine and an acidic polysaccharide or a method of preparing them. The specific mechanism for taste-masking, indicated in claims and argued by applicant as the distinguishing limitation, does not render the claimed composition novel over prior art compositions containing the same ingredients and suitable for oral use.

Applicant argues that by filing Evidences A-D they have established that "the bitter taste of donepezil hydrochloride was not even known at the time of the priority dates of the present application". Applicant disagrees with the Examiners position on obviousness and state MPEP 2141 to support their argument that "the focus when making a determination of obviousness should be on what a person of ordinary skill in the pertinent art would have known at the time of the invention….". This is not found persuasive. In response to arguments regarding obviousness, The Supreme Court in KSR reaffirmed the familiar framework for determining obviousness as set forth in Graham v. John Deere Co. (383 U.S. 1, 148 USPQ 459 (1966)), but stated that the Federal Circuit had erred by applying the teaching-suggestion-motivation (TSM) test in an overly rigid and formalistic way. KSR, 550 U.S. 82 USPQ2d at 1391. Specifically, the Supreme Court stated that the Federal Circuit had erred in four ways:

(1) "by holding that courts and patent examiners should look only to the problem the patentee was trying to solve ".

(2) by assuming "that a person of ordinary skill attempting to solve a problem will be led only to those elements of prior art designed to solve the same problem"

(3) by concluding "that a patent claim cannot be proved obvious merely by showing that the combination of elements was obvious to try'".

(4) by overemphasizing "the risk of courts and patent examiners falling prey to hindsight bias" and as a result applying "[r]igid preventative rules that deny factfinders recourse to common sense".

In KSR, the Supreme Court particularly emphasized principles based on its precedent that "[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.". Also, the Court recognized that when a patent claims a structure already known in the prior art that is altered by the mere substitution of one element for another known in the field, the combination must do more than yield a predictable result."

In this application, the obviousness has been shown. Tai has clearly shown that an active agent with bitter taste can be combined with a polymer such as carrageenan to form solid particles (microcapsules) that are not bitter and dissolve in the gastric fluid (i.e. do not dissolve in the oral cavity).

Applicant argues against the Double Patenting rejection of claims over US Patent 6,576,677 to Ukai et al in view of Tai. Applicant argues that "the mechanism of preventing a bitter taste of donepezil hydrochloride in the claimed invention is different than that recited in the reference claims. This is not persuasive either. Reference claims are drawn to compositions comprising active agents such as donepaezil hydrochloride

and a component such as polyvinylpyrrolidone and a method of alleviating an unpleasant taste of a medicament with unpleasant taste such as donepaezil hydrochloride by adding thereto a component such as polyvinylpyrrolidone. Tai teaches formulations and method of resolving the unpleasant taste of medicaments such as sucralfate by combining it with a suitable polymer such as polyvinylpyrrolidone or carrageenan. Thus it would have been obvious to one of ordinary skill in the art to have substituted carrageenan for polyvinylpyrrolidone with reasonable expectation of obtaining the same results. The mechanism of preventing a bitter taste is not a distinguishing factor since the end result is the same.

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINA HAGHIGHATIAN whose telephone number is (571)272-0615. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mina Haghighatian/

Mina Haghighatian
Primary Examiner
Art Unit 1616